Amyloidosis presenting in the urethra

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Primary localized amyloidosis (amyloid tumour) of the urethra is a rare entity with barely more than 15 reported cases. The urologist and surgical pathologist should be aware of its features since the diagnosis can be easily missed on examination of small biopsy specimens. Its recognition is important since it usually resembles carcinoma in its clinical manifestations, but commonly demonstrates a relatively indolent behaviour and can often be treated conservatively.

Case report

In July 1985, a 38-year-old white man was referred for urological consultation by his family doctor because of a 2-week history of intermittent bloody urethral discharge accompanied by discomfort in the terminal portion of the urethra. His symptoms had not responded to a week's course of tetracycline therapy. There was no prior history of genitourinary or other medical problems, or of any significant family medical history. Examination of the external genitalia and prostate was normal. The patient underwent cystoscopy, which revealed a segment with an irregular mucosal surface with areas of reddening in the penile urethra (Figure 1). This abnormality extended from just within the fossa navicularis distally for about 1 cm proximal to it. The bladder appeared normal. The abnormal area was biopsied, following which a tentative diagnosis of amyloidosis was made. Biopsies of bladder and rectum were taken several days later and stained negatively for amyloid.

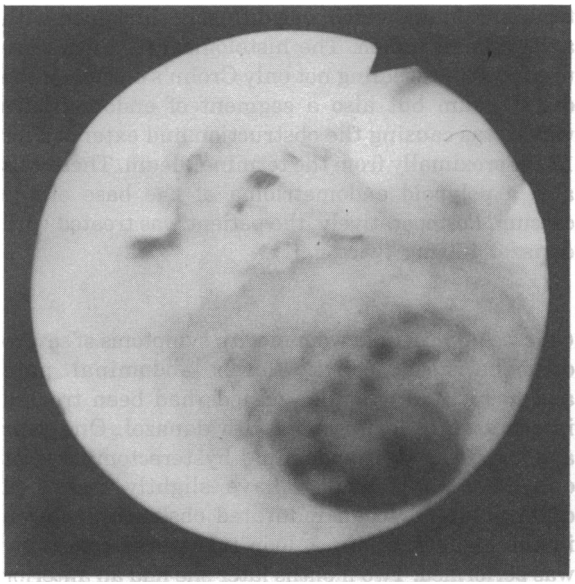

Figure 1. Cystoscopic appearance of penile urethra: Note the shaggy irregular mucosa with areas of reddening

Microscopic findings: At first glance, the pale staining amorphous material seen deep to the urethral epithelium (Figure 2) could easily have been mistaken for necrotic tissue, such as could be found on the surface of a neoplasm or sloughed off in an infection. However, it stained positively with Congo red for amyloid (i.e. orange), demonstrating lime green birefringence with polarized light (Figure 3) and metachromasia with crystal violet. The amyloid was deposited in two patterns: (*a*) in solid globules and diffusely beneath the urethral epithelium, elevating

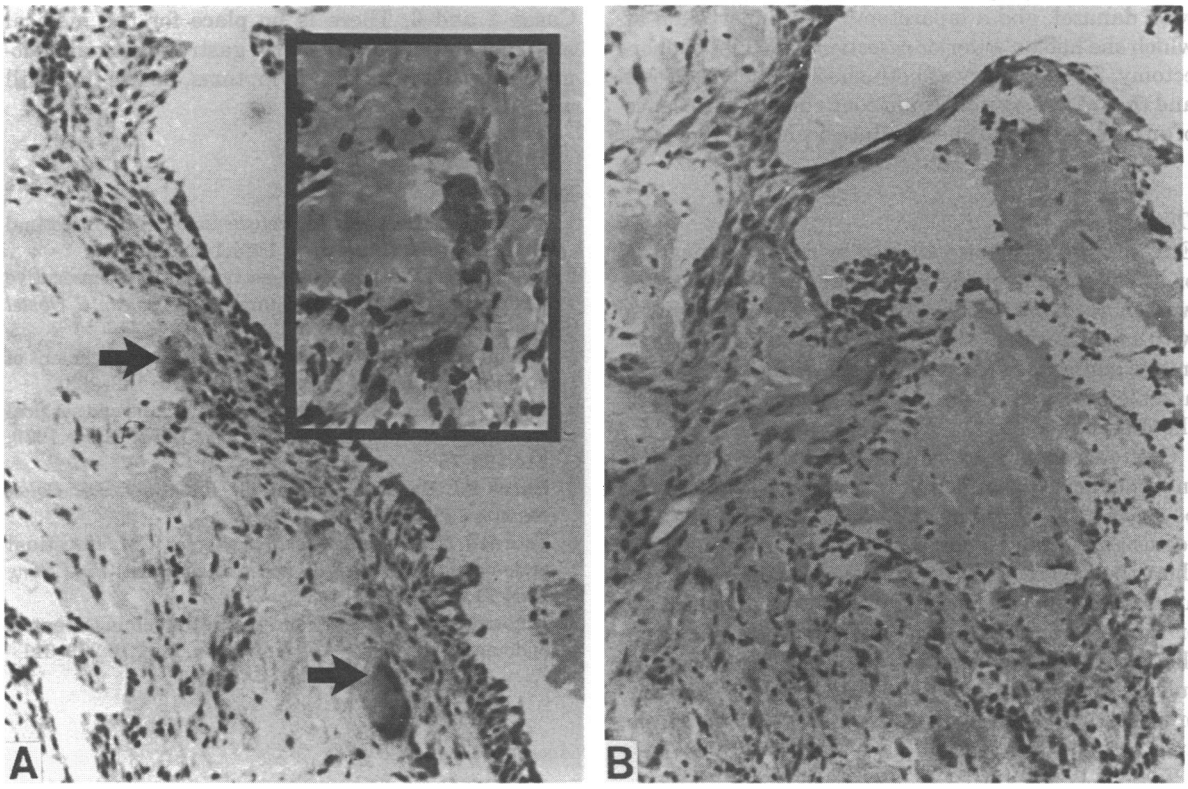

Figure 2. Sections of urethral biopsies demonstrating (A) diffuse pale amorphous infiltrate and giant cells (arrows and inset), and (B) globular masses of amyloid elevating and disrupting urothelium. (H&E, original magnification ×125, inset ×500)

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Figure 3. Congo red stain demonstrates birefringent amyloid in urethral stroma, when viewed with polarized light. (Original magnification ×125)

and disrupting it, causing squamous metaplasia, provoking a giant cell reaction and widening the spaces between connective tissue cells (Figure 2); and (*b*) in the walls of deeper blood vessels. Electronmicroscopy demonstrated fibrils characteristic of amyloid.

Discussion

This entity is best classified as 'primary localized amyloidosis of the urethra'[1] and was first described by Tilp[2] in 1909 in an autopsy case. There have been more than 15 additional, mostly individual, case reports from autopsy and surgical specimens.

A recent review[3] indicates that, unlike its more common counterpart in the bladder, which has been reported in both sexes, urethral amyloidosis presenting as a clinical entity has only been seen in males. To date, it has not been associated with the presence of, or later development of, generalized primary or secondary amyloidosis, as occurs in some bladder cases[4], this being an important potential prognostic difference.

The most common presenting symptom of urethral amyloidosis is haemorrhage, as a bloody urethral discharge or as haematuria. This is similar to tumefactive amyloid in the bladder, which most often presents with haematuria (sometimes following the trauma of cystoscopy). However, massive and sometimes fatal bleeding has been reported only from bladder lesions[4]. Probably the prime cause of bleeding is ulceration over the tumefactive amyloid deposits, possibly aggravated by infection (which may precede the amyloid). Also, deposition of amyloid in or around the walls of blood vessels may interfere with their normal contractility.

Next most common in the urethra are symptoms related to obstruction of urinary flow. There may be a stricture, a mucosal irregularity, or a mass may be palpable or seen with an endoscope. These are all clinical features shared by neoplastic growth, most commonly carcinoma, which is the usual preoperative or pre-biopsy diagnosis.

Amyloidosis is most commonly unifocal but may be multifocal in the urethra, rarely also in the bladder[5]. Any portion of the urethra may be affected.

The histological findings in our case are similar to those in other reported examples, although sometimes there is a marked associated chronic inflammatory cell infiltrate, and giant cell reaction is not always present.

Recent studies[6] suggest that the amyloid in most, if not all, of these cases is of immunocytic origin, possibly produced by adjacent monoclonal plasmacytic infiltrates resulting from local infection. A few cases have had a history of gonococcal or non-gonococcal urethritis[7].

The management of past cases has varied[3], depending largely on the individual characteristics of the lesions, from no treatment to open surgical resection of the tumour, usually with urethroplasty, but once with cystostomy. Some cases have required transurethral resection for relief of stricture or removal of tumour, or astringents or cauterization to control bleeding. One patient even underwent total urethrectomy for an erroneous clinical diagnosis of carcinoma[8].

Our patient has remained symptom-free, apart from mild discomfort on voiding, for 13 months following his urethral biopsies, without additional therapy.

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